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ABSTRACT

This status report is divided into eight sections. The first four represent the classical engineering or building aspects of bioengineering and deal with biomedical instrumentation, prosthetics, man-machine systems and computer and information systems. The next three sections are related to the scientific, intellectual and academic influence of bioengineering in the life sciences and concern classical engineering, physics, cybernetics or systems science, interactions between bioengineering and both engineering and biomedical curricula. Finally, Section 8 is concerned with future goals of bioengineering, in terms of directions, problems and probable ways in which needs may be met. (BB)

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Biomedical Engineering

Status of Research in Biomedical Engineering 1968

a report by the

ENGINEERING IN BIOLOGY AND MEDICINE TRAINING COMMITTEE

of the

National Institute of General Medical Sciences
National Institutes of Health

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in

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NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

NATIONAL INSTITUTES OF HEALTH

FOREWORD

This is the second year that a number of our advisory committees have favored us with reports of the status of research in their respective areas of competence. As originally conceived, the primary purpose of these reports was to aid in keeping the Institute staff well informed so that the latest information concerning special areas of science could be focused upon problems of immediate importance and upon long-range program planning.

The responsibilities of this Institute are different from those of a disease-oriented Institute in that our general mission is to support research and research training in the health sciences and in certain interdisciplinary fields rather than to support research directly concerned with a disease or a group of diseases otherwise the major concern of another Institute.

These responsibilities are complex, diverse, and interrelated in terms of the dynamics of the fields supported. We must be prepared to deal with the problems of a large number of scientific fields and to operate in each at either a general or "in depth" level as the situation demands. For these reasons, a research status report, or if you will, an annual summing up by each of our committees of expert consultants responsible for advising us on a scientific field or discipline, has become particularly useful to this Institute.

For example, a primary mission recently assigned this Institute is to survey various biomedical science areas to assess their vigor, state of health, and content. Research status reports have contributed materially to these studies, since they deal with recent developments, problems, and discernible trends in a field. In fact, in several instances, research status reports have indicated wherein the developments and trends in one scientific field pointed to an intercept course with another. Such information is particularly useful if known in advance, for measures can then be taken to coordinate future developments to the mutual advantage of all areas concerned.

Additionally, research status reports seemingly fill still another need which was not foreseen. Various top-echelon government science advisory groups have found these reports helpful as have high administrative officials in the academic field, especially those charged with planning the organization and staffing of medical schools. Presumably the interest of both of these groups is centered primarily on the future, as is the general approach in all research status reports.

We are grateful for this report by the Engineering in Biology and Medicine Training Committee. I am sure it will help further the work of this Institute.

Frederick L. Stone, Ph. D.
Director, National Institute
of General Medical Sciences

BIOMEDICAL ENGINEERING

Contents

	Page
Foreword	i
Contributing Consultants	iii
Engineering in Biology and Medicine Training Committee	iv
Introduction	1
I. Biomedical Instrumentation	2
II. Prosthetics	9
III. Man-Machine Systems and Environmental Control	14
IV. Computers and Information Systems	19
V. Engineering Physics	32
VI. Cybernetics or Systems Science	40
VII. Education	47
VIII. Goals	52
Bibliography	70

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INTRODUCTION

Bioengineering, biomedical engineering, or engineering for biology and medicine is that field which deals with the interaction between the engineering sciences and biology and medicine. Because engineering is really two fields--building, using scientific principles, and analysis of complex mechanisms--bioengineering also is two fields: one concerned with building devices for biology and medicine, especially the development of instrumentation and data processing systems; and the other, the analysis of complex biological systems by means of the application of engineering science. At the present time, biomedical engineering is experiencing a rapid and vigorous developmental phase in many university, government, and industrial laboratories throughout the country, especially those that are in the forefront of scientific and engineering teaching and development.

This status report is divided into eight sections. The first four represent the classical engineering or building aspects of bioengineering. It is perhaps the area that most people think of primarily when biomedical engineering is mentioned. Section I deals with biomedical instrumentation, including transducers for both measurement and control, complex transducers, and systems of instrumentation. Section II discusses prosthetics, or the field of artificial organs. Section III, on man-machine systems, includes the interaction of man with machines for working and the interaction of man with his environment so as to control material in the environment rather than pollute it. Section IV, on computers and information systems, differs

from the previous ones in being less hardware-oriented and more information systems-oriented. It stresses the important impact of digital computers in all new technical fields.

The next three sections are related to the scientific, intellectual, and academic influence of bioengineering in the life sciences. Section V deals with classical engineering physics applied to such areas as cardiovascular hemodynamics and cardiac electrical field studies. Section VI, on cybernetics or systems science, includes control, information theory, the analysis of physiological, biophysical, and biochemical systems with engineering conceptual methods, and bionics, which has to do with the use of biological principles in widening concepts of engineering design. Section VII, on education, deals with interactions between bioengineering and both engineering and biomedical curricula, as well as with bioengineering training programs, whose academic disciplinary status is still unresolved.

Finally, Section VIII is concerned with future goals of bioengineering both in terms of directions, problems, and probable ways in which needs may be met. It suggests certain foci of interest that may be helpful in planning efforts attempting to utilize limited resources effectively.

The preparation of this report was considerably aided by contributions and critical review by university training program directors and bioengineers throughout the nation. Nevertheless, many of the leading active workers in the field must of course be unmentioned in this brief report which chose only scattered works as examples and did not attempt to review or evaluate the field in depth.

I. BIOMEDICAL INSTRUMENTATION

A. General Aspects

Development of bioinstrumentation is the sine qua non of

bioengineering. Measurement of such biological quantities as the pressure, temperature, velocity, and constituency of the blood, the capacity, frequency, sounds, and electrical activity of the heart are routine. Less frequently we measure the length, force, and compliance of skeletal muscle, the position of the tongue, the impedance of the brain, the motility of the gut, and many other variables. The transducers are mechanical, optical, acoustical, chemical, resistive, inductive, capacitive, photoelectric, piezoelectric, and thermoelectric. A lengthy bibliography to 1964 appears in the review paper by Geddes [1].

The considerable diversity of medical instrumentation and its social and commercial importance have made this area of design an important one for the bioengineer. In addition, the technical aspects of instrumenting a living organism provide an intellectual challenge, since state-of-the-art capabilities are often stretched a little in such applications. Design criteria relating to signal-to-noise ratio, frequency response, sensitivity, impedance levels, reliability, stability, safety, size, and power requirements are somewhat more exacting for biomedical instrumentation than for many other types. Noise arises from muscle tremor and galvanic effects in addition to the random thermal sources present in all instruments. The slowly-varying nature of metabolic processes imposes strict requirements on low frequency characteristics. Many bioelectric phenomena (e.g., EEG) yield body-surface potentials in microvolts, and amplification is necessary. The source impedances of transducers may be measured in terms of megohms (e.g., microelectrodes). Currents delivered to human subjects in the event of electronic failure must be less than 1 milliamp. Implanted instruments must

be reliable and long-lived, stable, safe, and small. These are a few of the features that have characterized medical instrumentation.

Finally, it is appropriate to note the complexity of instrumentation systems in which the individual transducers are interconnected for the simultaneous monitoring of respiratory, cardiovascular, and renal function along with blood, oxygen and pH. Such systems are common in operating theatres and play a vital role during open-heart surgery and post-operative intensive care. Instrumentation complexes linked to digital computers are now being proposed for management of non-surgical patients critically ill from myocardial or cerebral infarction. Entire symposia are being devoted to this subject and further discussion will appear in Section IV.

B. Active Transducers

The previous paragraphs dealt with passive transducers, i.e., those that receive energy from biological sources and thus tell something of body function. Besides these there are active transducers that deliver power to the body for diagnosis, therapy, and control. The familiar medical X-ray is an excellent example of the application of external energy to diagnosis; but ionizing radiation is used therapeutically as well in the treatment of cancer. Here, bioengineers are not only concerned with source design but also with the dosimetric calculations from external collimated sources and implanted radioactive needles. In a similar way, microwave and infrared energy are used in diathermy instruments. Currently, changes in volume (e.g., respiratory)

are measured by passing a high-frequency current through the body and noting the change in impedance. Currents delivered to the skull can induce anesthesia, and electrical stimulation of the carotid nerves can be used to control severe hypertension in a manner that duplicates the normal physiological method of control. (See Fig. 1.)

The exciting advances being made in active transducers include the use of ultrasound, lasers, fiber optics, microminiaturization and implantation, telemetry, cryogenics, prosthetics, and the complex instrumentation systems involved in extracorporeal maintenance of circulatory or renal function. The use of ultrasound is an example. Even though general ultrasonic neurosurgery has recently been abandoned in the United States because of the necessity of removing large amounts of cranial bone, the method is still important for routine destruction of labyrinth cells in treating Meniere's disease.

The diagnostic application of ultrasound has been much more rewarding. Echosonography is being used to visualize soft tissues of the body in diagnosing carcinoma of the breast, cirrhosis and carcinoma of the liver, renal cysts, intraocular tumors, retina detachment, and hemorrhage. Motion of the mitral valve leaflets is easily seen in ultrasonic scans, allowing diagnosis of mitral stenosis as well as insufficiency. Although sound reflection in the skull bone poses great difficulties, echoencephalograms can show the lateral ventricles and other brain structures, and shifts in midline echo patterns indicate unilateral enlargement processes. These examples of the applications of echo-ranging ultrasonics to medicine are now well described in the Swedish literature [3], [4] and our own [5], [6].

The Doppler shift in frequency produced when the reflecting surface is in motion has also been successfully employed in measuring blood flow transcutaneously [7].

An ultrasonic microscope is under development by Jacobs, whose work in image-processing is well-known [8]. An excellent ultrasonics bibliography is contained in a review paper by Jacobs [9]. Roth [10] has proposed another pair of interesting imaging devices (for radiographic pictures) in which the display device adds full color or isometric aspect, thus enhancing the information content assimilated by the viewer.

The increasing use of ultrasonic body scanning will require further basic research on ultrasonic properties of biological tissue. Such basic biophysical research on absorption and velocity measurements in blood, fat, muscle, and bone has been done by Edmonds [11], [12].

The laser shows promise as an effective instrument for highly focused destruction of malignant cells in surgical cancer therapy. Two problems still under study are the effects to surrounding tissue and the difficulty of collecting airborne malignant tissue spattered by the laser impact. Neodymium and ruby lasers have been compared with noncoherent light sources (Xenon flash lamp) and nonthermal effects have thereby been isolated [13]. These include molecular depolarization, resonance absorption, and ultrasonic oscillations. Vacuum-operated plume traps are being designed to prevent the spread of particulate matter from the treatment site [14]. Besides cancer therapy, laser surgery shows promise in dermatology, opthalmology, and dentistry. For the future, it is expected that diagnostic uses of the laser will soon

be developed. One example in this area is the recent use by Bowman and Blume [15] of a scattered laser beam for bacteria colony counting; a second example is the work of Baker and Johnston in determining molecular alignment of amoebic cytoplasm [16].

Other optical applications in bioengineering have been the use of bright light to transilluminate infant skulls and the use of flexible light pipes with separate illuminating and viewing fibers for visualization of internal organs. The opacity of blood to visible light may suggest a marriage of lasers and fiber optics at a wavelength suitable for viewing even the inside of the heart.

The most significant electronic development of this decade, integrated microminiature circuits, has a direct application to bioengineering of implantable instruments for metering and control. Ko [17] has proposed the implantable stimulator (Fig. 2) which derives its control electromagnetically through the skin. The implanted cardiac pacemaker, besides being the most important example of implant electronics, has also led to some serious engineering analyses of biological impedance and the electrode-myocardial interface. Schwan's [18] pioneering work in this area will be described in Section V.

One of the serious obstacles remaining in the use of integrated circuits for implants is the development of suitably small power sources. Biochemical generation of power internally or magnetic coupling of power through the skin has been suggested and Roth has conceived of a device extracting energy from diaphragmatic movement.

Closely related to implant electronics is the remote telemetry of physiological function pioneered by Mac-Kay and the development of prosthetic instruments, to be discussed in Section II.

In addition to laser surgery mentioned earlier, two other modern engineering developments have been applied to surgery: the use of the intense, localized heat of a plasma arc scalpel for bloodless surgery [19] and the use of the extremely cold temperature of a cryogenic probe.

C. Further Development

Although trends in biomedical instrumentation have been toward better display and more quantitative measurement, it is not always easy to gain acceptance for newer, more expensive and more complicated equipment. The fact that the stethoscope is still in universal use is proof of the fact that we have not yet succeeded in providing a better way of handling heart sounds, despite considerable bioengineering effort. In order to make heart sounds quantitative and their analysis less subjective, bioengineers since Einthoven [20] have been interested in phonocardiographic recording. To reduce the loud low-frequencies and enhance the soft highs which are thought to contain much of the information of medical interest, Bekkering [21] and others designed high-pass filters. Although the Bell Telephone Laboratories' "visible speech" method [22] of using a scanning bandpass filter to record frequency content versus time has not replaced the oscillographic display with sets of filters, nevertheless the search for better methods of display continues. No doubt, digital computer spectral analysis will soon evolve as a sophisticated technique for diagnosis of heart sounds that will be routine in advanced laboratories.

Future growth in the area of biomedical instrumentation will involve the application of more sophisticated methods of signal

processing, display, and storage, taking advantage of integrated circuits and digital techniques. In fact, incorporation of a digital computer for high-speed on-line acquisition, decision, and even control represents a sort of ultimate in instrumentation which is now within reach of some experimenters. And, in research, as medicine relates bodily manifestation more and more to intra-and inter- cellular processes, it will become necessary to use some of the modern molecular biological instruments, such as X-ray diffractometers, analytical ultracentrifuges, ultra- and electron microscopes and optical scattering instruments. Interpretation of data from these will necessitate considerable computation and increase the employment of digital computers.

II. PROSTHETICS

Closely related to instrumentation are the artificial devices being engineered to replace, temporarily or permanently, essential body organs or structures. The chief design problem with these prosthetic devices involves materials (covered in more detail in Section V). Other interesting engineering aspects that appear as the complexity of the prosthesis increases include control and power supply problems as well as problems of maintenance and repair.

The following terminology has been suggested for cardiac prosthetics [23]. Restorative prosthetics are prosthetics used to correct existing heart defects, but which do not supplement heart functions. Included here would be intracardiac patches, prosthetic valves, and pacemakers. Cardiopulmonary bypass units are short-term emergency blood pumps and

oxygenators which permit temporary heart bypass to permit restorative operative procedures. Circulatory assist devices are of two types: external units without vascular connections, and external units with vascular connections. These latter include devices for diastolic augmentation, such as arterial pumps and counter pulsers, systemic shunt devices, such as venous to arterial shunt pumps, and partial left heart bypass units. Implantable circulatory assist devices include implanted partial left heart bypasses wherein the pump is internally situated within the closed chest and internal heart massage units--devices which encapsulate one or both ventricles to augment ventricular work. Artificial hearts are total cardiac replacements, i.e., hearts designed to take over complete cardiac functions.

Klain et al. [24] have recently tested and evaluated the different aortic and mitral valves. The aortic valves used for this study were: Gott, Teardrop, Starr-Edwards, Leaflet, Pin, and Heavy Teflon type. The mitral valves used were: Gott, Teardrop, Hammersmith, Starr-Edwards, and Heavy Teflon type. They have concluded that the Starr-Edwards and Teardrop valves are most suitable for aortic position and the Gott valve is better than the others in mitral position.

Most pacemakers in current use are of the fixed-rate type powered by mercury cells and stimulating via electrodes attached directly to the heart or passed through a peripheral vein. Such pacemakers can reduce the mortality of complete heart block by nearly 60 percent and 9 out of every 10 paced patients are now likely to survive at least the first 12 months of treatment [25]. A few implanted pacemakers have continued functioning for over four years, but most need replacement

well before the calculated battery life-time. Many failures were due to difficulties with electrodes (fracture, malposition, loss of satisfactory contact with the pacemaker), infection, or high threshold for stimulation. More sophisticated pacemakers are being developed to overcome disadvantages of the simple fixed-rate units. Further development of new types of pacemakers is needed to improve reliability.

The mechanical auxiliary ventricle developed by Kantrowitz [26] is a plastic, airpowered, avalvular, synchronous pump permanently implanted in the chest. The prosthesis functions in series with the left ventricle, appreciably reducing its work and becomes, in effect, a booster heart. Other electronically controlled implantable auxiliary ventricles have been developed [27], [28].

The various mechanical and biological problems with a totally implantable heart have been recently reviewed by Burns et al. [23]. The two major problems involved are those of preventing clot formation and the selection or development of proper materials for blood pumping chambers. The embolic and thrombolic phenomena currently pose the greatest threat to the overall success of the artificial heart development, especially any total replacement.

The human heart has the infinite advantage of having self-repair characteristics. Biological systems are able, to a large degree, to repair defects created by fatigue and to respond by strengthening stress points. Unfortunately, these capabilities are not possessed by any man-made materials currently available.

The development of the artificial kidney has now made possible repetitive hemodialysis and the sustaining of life of chronic kidney

failure patients. In recent years, considerable attention has been focused on the problems of simplifying and reducing the size of artificial kidneys. A much-desired objective in this regard is an artificial kidney that can be worn by the patient [29]. LeVine and La Course [30] have proposed an artificial kidney on the order of about 2 cm in diameter and 10 cm in length using multicomponent microcapsules capable of eliminating urea, uric acid, creatine and ammonium ions. Further research is needed in developing better membranes and designing low-cost artificial kidney systems [31].

Some recent mathematical modeling of hemodialysis has been done by Baker. An analog computer approach shows that a programmed exponential increase in dialysance by increments should limit the intra- to extra- cellular urea gradient and avoid the "disequilibrium syndrome" that occurs during rapid hemodialysis.

Cooney et al. [32] have developed procedures for purification and concentration of thoracic duct lymph and similar fluids. This is preparatory to a study of large and small solute clearance in artificial kidneys.

The ever-increasing use of open heart surgery has intensified the search for a simple and effective heart-lung machine. The development of techniques for the extracorporeal oxygenation of blood has two objectives: 1) to oxygenate venous blood to the level which is usually found in the pulmonary veins and provide adequate mechanisms for the removal of carbon dioxide and 2) to ensure that the physical and chemical properties of the blood are not changed. Most artificial lungs currently in use during extracorporeal circulation contact the

blood directly with the gas phase. Although this procedure is highly efficient for mass transfer, it is known to cause toxic denaturation of the blood, prohibiting prolonged use [33], [34].

The introduction of a semipermeable membrane between the blood and gas reduces significantly the damage to the blood; however, it increases the mass transfer resistance. Various types of oxygenators have been suggested [33], [35]. The major stumbling block in the design of oxygenators has been the lack of a semipermeable membrane capable of passing oxygen and carbon dioxide in sufficient amount to maintain life over long periods.

Mechanical devices have been devised for many years to assist persons who have been deprived of some measure of normal physical ability [36]-[38]. The limb prostheses which are now clinically available, in general, have the following shortcomings:

1) The prostheses have far fewer degrees of freedom than the normal limb for which they are intended to substitute.
2) The controls for a given prosthesis motion are not related to the actions of a normal person which cause the corresponding motion of a normal limb.
3) The only sensation which the amputee receives from the prosthesis is that which he can obtain from visual observation of its performance.

Bioelectric control of prosthesis using the EMG signals from the surface of the skin offers the possibility that control of the prosthesis action can be similar to control of the corresponding body action [39], [40]. It is clear that new developments are needed in

the way in which amputees must control their prostheses. The interface between the man and his prosthesis must be made less abrupt.

A well-known prosthetic device--the contact lens--has been studied by Hill and Fatt [41]. Their technique for measuring O_2 and CO_2 (shown in Fig. 4) has demonstrated the necessity for a loose fit, in order that proper gas exchange with the cornea can occur.

III. MAN-MACHINE SYSTEMS AND ENVIRONMENTAL CONTROL

A. Man-Machine Systems

Traditional disciplines have dealt with man in isolation and with machines in isolation. Physiology and psychology have produced an extensive body of knowledge about the human body and human behavior in general. Similarly the traditional engineering disciplines have studied materials, structures, systems, etc., in general. However, the material products of our culture provide the context in which and with which man lives and behaves. This implies that the characteristics of the user are an important consideration in the design of a machine and the characteristics of the machine are an important influence on the operator. It is natural, then, to describe the machine and the man as part of a total system which comprises both.

The man-machine system which has received the most intensive study is the pilot-aircraft system. The conception of the operator as a component in the overall man-machine system was discussed by Craik [42] and the development of very high-performance military machines made the intensive analytic study of the human controller inevitable. The Defense Department is by far the principal sponsor of this class of

investigation. Descriptions of the pilot as controller have clear implications for machine design [43], [44], but such descriptions necessarily fail to be comprehensive. Though the pilot may for some purposes be profitably regarded as a transfer function in a complex system, a realistic representation of his full range of performance would probably be mathematically impossible. Though there is a vast amount of knowledge of the human operator, an even greater amount remains to be discovered. The characteristics of the operator in receiving and transforming inputs in all sensory modalities are clearly relevant to man-machine system design [45]. Experimental determinations of the control characteristics of the operator always make simplifying assumptions and standardizations of the characteristics of the input. The work that is done at the behavioral or neurophysiological level on human sensory data processing in vision, audition, kinesthesis, cutaneous senses, vestibular sense, and perhaps even in taste and smell, has potential relevance to man-machine system design. In addition, such factors as work cycle, fatigue, diurnal cycle, attention, memory span, and motivation are known to have powerful effects on human performance generally, but have not yet been systematically evaluated and analytically described in terms of system function. It is more usual to use simulators to determine the effects of these factors on critical performance variables, such as landing speed. Nevertheless, more and more comprehensive knowledge along these lines is accumulating and filtering through to the level of man-machine system design and analytic description of the operator (e.g., Young and Stark [46]) seems to be more in accord with known characteristics of human short-term attention and memory.

There will always be need for a great deal of purely empirical work towards optimization of man-machine interaction. For example, no theoretical basis need be established for the relative efficiency and human preference for various telephone dialing arrangements [47]. Fig. 5 from Deininger [47] shows results of this kind of applications-oriented research.

B. Safety

To make a man-machine system safe probably means making it better in terms of integrating man and machine characteristics. It seems very likely that improvement in operator-vehicle systems will accelerate under the stimulus of public concern for safety, both in commercial aircraft and in automobiles. Large safety improvements will probably come from changes in the machine--in materials (e.g., better padding, stronger alloys), components (e.g., puncture-proof tires), subsystems (e.g., better brakes), etc. These "hardware" improvements might be contrasted with "software" improvement predicted on man-machine interaction factors, which may eventually bring even larger gains in safety.

On the approaches to some expressways, there are displays which inform the motorist of the conditions he will encounter (dense traffic, accident, route blocked, light traffic, etc.) and he may elect to take a different route. On his radio he can receive traffic reports and advice on routes from a helicopter pilot viewing the whole traffic system. Such "software" approaches of traffic control probably prevent more highway deaths than improvements of "hardware," though empirical support for this view would be hard to obtain. However, modeling of the traffic system is providing acceptable evidence which has entered into

policy and planning decisions. A useful review of such modeling is given by Gazis [48]. Clearly, great opportunities exist to improve the flow of traffic. A traffic control system is conceivable in which every driver's position and destination would be known and optimum routing and speed would be calculated and transmitted to each driver. Indeed, this describes the air traffic control system. The greater density of ground traffic control would call for the use of a large computer in every city and a very large investment in communications.

C. Environment

Since an organism's well-being is directly related to its environment, it is only natural that, with modern technology's ability to modify the local environment and with its ability to place an organism in an unusual environment, there should be a large body of biomedical engineering literature devoted to environmental study.

One of the most unfortunate aspects of the development of new technology has been the pollution of both air and water. The magnitude of the problem has long been recognized and organizations, publications, and meetings are now being devoted to this subject. For instance, the Air Pollution Control Association now publishes the APCA Abstracts and the European Conference on Air Pollution held in Strasbourg in 1964 has just recently published its proceedings.

Extensive studies are now being undertaken to define the sources of air pollution. Automobile fumes have been studied recently [49]-[51], as have industrial sources [52], [53] and radioactive sources [54]. A further source of pollution has been the increasing use of pesticides and herbicides [55]. The effects of all of these different types of pollution

of the environment need to be defined and probably more work has been done on the pneumoconioses than any other facet of the problem [56], [57]. The biologic effects of radiation have also been a fertile field for investigation recently [58], [59].

Although the effects of heat and cold on the human organism have long been studied [60], [61] and considerable study has been devoted to the effects of alterations of pressure [62], more recently modern engineering has developed several new sources of energy whose effects on biologic tissues are just beginning to be studied. These include microwaves as well as ultrasound [63]-[65].

With the advent of modern high-speed travel, still further areas of interaction between biology and engineering have developed. Such areas include the problems of noise and its control [66] and the problems of vibration [67], [68]. One of the most interesting results of this new mode of travel has been the dissociation between the metabolic diurnal rhythm of the traveler and the actual local time [69], [70].

However challenging the environmental problems of the earth-bound may be, travel in outer space has made for countless new possibilities. Studies are currently underway merely to define the nature of the new conditions to be found [71], [72]. The proposed investigation or lunar samples include a number of studies in the Bioscience Program for biochemical and organic analyses [73]. The effect of space travel on man has been a fruitful field for study [74], [75] and considerable effort has been expended to provide environmental simulation for crew training [76]. The simulation of space conditions here on earth has been an important aspect of this study. Vacuum technology is such

that in the last 10 years achievable vacuums have gone from 10^{-6} to 10^{-12} torr [77]. Alien surfaces have been modeled [78] and thermal modeling has been undertaken [79], [80]. Even solar emission has been modeled [81].

Finally, the possibilities of interplanetary travel have raised other environmental questions. Not only is there the question of the presence of life on other planets [82], [83], but one might wonder about planets that would support human life [84], [85] In the latter situation one would have to consider the adaptation of man as a species to differing extraterrestrial habitats [86].

IV. COMPUTERS AND INFORMATION SYSTEMS

The previous sections of this report dealt with design of instruments, prosthetics, and human-hardware interfaces. An equally important area of bioengineering deals with analysis of biosystems. Overlapping these two fields are the digital computers that serve sometimes as fast, sophisticated measuring instruments and other times as analyzers and problem solvers. This section concerns itself with the bioengineering use of computers.

A. Numerical Uses--Data Handling and Analysis

This was perhaps the first use of digital computers in medicine with the computer playing much the same role it did in commercial applications. Much of this data handling is of the service type and will be expounded upon in Section IV-B. Presently we will consider data handling from biological environments such as laboratory preparations. Much such data must be subjected to statistical analysis because of noise or stochastic processes inherent in the biological system. The data are usually taken with regard to investigator facility and ease of recording. Therefore, when digital

processing is necessitated, data must be put in more suitable forms, e.g., tabulated data are preferred to analog signals when conversion equipment is not extensively available.

Much effort has been directed at packaged programs to perform pre-analysis of data according to some statistical criteria. Dixon [87] has published an extensive list of programs especially suited for biomedical work. These programs range from simple averaging to regression analysis of time signals. The programs treat data as a data matrix acquired in real-time and stored for later off-line analysis. Up to 10^7 experiment-variable locations can be handled for the high-variable type of experiment.

More recently [88], on-line experimentation and analysis have become necessary because of their advantages of not requiring secondary data handling capabilities which become unwieldy at high data rates. The advent of the process control (PC) computer with ample analog-to-digital conversion equipment has been a boon to on-line experimentation. However, the PC computer is more realistically cast as a pre-processor for a more prodigious machine, since the PC machine usually lacks the computation hardware for rapid on-line calculations.

Another approach to high data rate, on-line experimentation has been the special-purpose computer of which the LINC is an early example [89]. The medical computer field abounds with special-purpose machines capable of performing specialized tasks. They do this by giving away almost all flexibility to the end of a few narrow performance goals. When the experimenter's goals are well defined such machines could be the best choice for data acquisition and processing.

B. Simulation

Biological model simulation or, as Bartholomay calls it, "in numero" studies using analog, digital, and hybrid computers, has a relatively long history in the biomedical engineering field. The use of analog computers pre-dates the digital machines, going back to the late 1930's [90]. One of the first attempts at biological system simulation by analog computer was made by Grodins [91] in 1954. Defores [92] in 1960 and Horgan [93] in 1962 extended Grodins' respiratory model significantly. Horgan has recently used the interesting technique of initially modeling the respiratory system on an analog computer and then turning to digital simulation as the system dynamics become more familiar.

The logical branching ability of the digital computer is used advantageously in neural networks modeling as a second example of non-numerical computer uses. In this field, more than any other, the computer is essential because of the large numbers of elements considered [94].

It is but a small step from neural networks to computer programs used for theories of higher mental processes [95] and a smaller step from mental processes to the sociological behavior found in ecological systems [96]. In the "branch" -type programs, large memory and a great degree of flexibility are essential, but high arithmetic accuracy is not very important. Some sort of pictorial display is also essential. Real branching systems or ecological regimes of any complexity require the highest capacity computer.

It has been apparent recently that the analog computer has been

used in the past and will be used in the future for biological simulations where knowledge of the parameters is complete. The close man-machine interface of the analog computer is especially suited for this purpose. However, as more information is accumulated about the system, greater system complexities are well suited for digital simulation because of the digital computer's greater simulation capacity [97]. This edge in capacity is overshadowed by the more complex man-machine interface so that it appears that the hybrid computer is a more flexible tool overall for such simulation [98]. The hybrid machine is a recent development reflecting a cross between an analog and a digital computer with the intention of utilizing the advantages of both. The analog computer is especially suited for integrating dynamic equations accurately over long integration ranges and for parameter optimization routines. The digital computer has large stored-memory capability, easy function storage facility, and rapid nonlinear calculation ability. Since most of the human functions are in some sense digitally controlled analog-output-type systems, the hybrid computer seems to be a natural choice for biological system simulation.

In a typical example suited for hybrid simulation [99], the memory and transport delay control (which represent the central nervous system and is of a digital nature) would be easily programmed on the digital computer complement while the retinal, ciliary, lens, and pupil dynamics (being analog-output devices) would appropriately be programmed on the analog complement.

Hybrid computation and simulation are presently being done mostly on special-purpose machines because of the absence of commercially available hybrid packages. It is expected that this picture is due to

change in the very near future as scientists and manufacturers more clearly see the advantages of such machines.

C. Signal Processing

Sophisticated biomedical computer programming has been heavily oriented toward electrocardiogram data processing, multiphasic patient screening, and control of psychiatric and psychological experiments.

In the ECG field, early workers immediately recognized the need for digital data processing from the great number of channels (12) ordinarily used in obtaining ECG's [100]. Data reduction procedures then came into common practice in the form of the so-called "vector leads," which reduced the channels to three but increased the information rates [101]. More modern computing facilities now enable workers to detect and analyze ECG data on line [102] and even hybrid computing has taken fast in this once completely digital field [103]. Digital filtering and averaging are becoming increasingly popular in EKG signal conditioning.

Fetal electrocardiography and phonocardiography have also taken advantage of computer techniques [104]. The computer is usually used in these applications for pre-processing simultaneous data channels [105].

EEG computer analysis is highly developed and even has been used in the Gemini space shots [106]. Since the amount of information in conventional multiple-channel EEG recordings is prodigious, many workers have used the computer to perform bilateral EEG analysis [107]. The advantage here is automatic data accumulation and the availability of rapid, many-pass analyses of the data at a later time.

D. Complex Instrumentation Systems

Routines for patient diagnosis via computer analysis began in the early 60's [108] and have continued with great momentum. The routines usually involve interaction with a physician or other qualified personnel in order to optimize the program's utility. One typical arrangement is proposed by Stark and Dickson [109].

The computer can also take on the role of a patient monitor, information converter, and environmental controller, all in one configuration [110]. Such a configuration usually requires a sophisticated, multi-interrupt level machine.

Another complex instrumentation system is found in neurophysiological studies [111]. In virtually all of these experiments to record simultaneously from many interrelated points in a given cerebral system, the instrument-computer interface requires sophisticated on-line programs to perform even the simplest averaging or autocorrelation or simpler forms of spectral analysis. This is because the on-line nature of the computer regime requires the experimenter to constantly monitor, inquire, and correct as possible, computer routines gone astray by experimental circumstances.

As an example of the diversity of work being done in a computer-oriented biomathematics group, Stacy [112] reports computer studies of respiratory dynamics, cardiac output, acute patient monitoring, digital filters, state diagrams of neural networks, oscillatory power dissipation in the pulmonary vessels, and Fourier analysis of interesophageal pressures.

Medical diagnosis by computer to a point approaching the work of

a practicing physician still seems distant even using the largest machine available. However, the work reported to date is quite encouraging. Mainly, it falls into three categories: computer-aids in diagnosis, computer-teaching of medical diagnosis, and statistical analysis of the diagnostic process [113]. Most effort has been directed at the first category and in particular at ECG diagnosis using both digital and hybrid machines.

E. Hospital Information Systems

In the process of caring for patients, a large quantity of information is generated which needs to be filed and organized in such a manner that it may readily be available when the need arises. It has been said that over one-quarter of the budget of a hospital goes into the handling of this information. It is only natural that the various disciplines such as computer sciences, systems science, and others which concern themselves with information manipulations should have an interest in hospital information systems.

There is a natural division of the business aspects of a hospital (such as billing patients, providing inventory control for the pharmacy, scheduling patients for clinics, and dealing with bed occupancy) from the more scientific aspects (such as collecting, recording, and storing for immediate access the actual pathophysiologic parameters of disease as recorded from patients). The business aspects have been dealt with by most hospitals with varying degrees of success. At the present time, there are probably few hospitals which do not use some type of automatic billing device in their finance office. More sophisticated business applications have been automated in very few hospitals. For example,

Children's Hospital in Boston has been able to increase average bed occupancy from 86.7 to 95 percent by automation. In our opinion, it is only a question of time before these more routine information-handling problems will be handled completely automatically and quite efficiently.

The problem of collecting, recording, and storing patient data is a more difficult one and it may take some time before systems of this type become truly operational. Such a system, to be truly worthwhile, should be operated in place of and not parallel with existing hospital facilities. The very quantity of patient data generated, the diverse locations where it is generated and needed, and its varied format add to the problems of dealing with it. Other contributing problems include the lack of background that most hospital staff have for dealing with automated data processing, the difficulty in keeping an automated data processing center in operation on a round-the-clock basis, and the real question of reliability of the system. With all these problems, there has been beginning work along these lines, most notably in the field of patient monitoring and particularly in constant care wards. Here the problem is much better defined, the information is generated and used in one location, and long-term data storage is not absolutely necessary. Furthermore, the patients are few in number and the staff using the system is small and can be specially trained.

Another result of the information explosion in medicine has been the rapid increase in the number of publications which must also be recorded for easy access. MEDLAR has been a stopgap attempt in this direction but is very definitely limited by the necessity of needing scientifically sophisticated coders to review titles and properly

categorize them. At the rate that medical literature is growing and because it is unlikely that such personnel will be easily available in increasingly large numbers, a fully automated system will become necessary in a relatively short period.

F. Man-Computer Interaction

The modern digital computer is a very unwieldy tool--its engineering for human use has been abysmally inadequate. For the last decade there has been general agreement about desirable improvements to permit a more effective man-machine system (e.g., Licklider) [114]. These are time-sharing to allow many users to take advantage of the speed and power of a large computer and perhaps each other's contributions as well; development of large, cheap, rapid-access memories; development of more powerful languages; and extension of I/O facilities. These improvements have been seen as steps toward increasing the problem-solving speed and power of the man-computer system by up-grading the quality and speed of information-transmission between the human and electronic components.

Time-sharing, "a juggling act of colossal proportion," has been achieved by computer manufacturers and independently by many scientific laboratories such as at Dartmouth, University of Utah (cf. Pryor and Warner [115]), Brain Research Institute, UCLA (cf. Rovner, Brown, and Kado [116]), and at MIT in project MAC (cf. Fano and Corbato [117]). There appears to be general agreement that small laboratory time-sharing systems may be adequate for their limited purposes but that a great deal of research and development remains to be done before the tremendous potential of time-sharing begins to be realized by large commercial systems.

The ferrite core is still the basic element in current large random-access memories. However, faster, larger-capacity memories are growing out of advances in various technologies, such as integrated circuits, superconductors, and thin films. Optical memories, which are attractive because they appear to be potentially the fastest, are also being developed.

More powerful information-processing languages have been developed, notably LISP [118], IPL [119], and FLPL [120]. The greatest effect of these has been to increase the power of the computer, but not the effectiveness of the man-computer system. New languages have made man-computer interaction more sophisticated but in general they have not facilitated man-computer interaction in the sense of reducing the necessary man-hours of training or the turn-around time. They have facilitated new problem-solving functions of the man-computer system but they have not facilitated the day-by-day problem-solving of the ordinary computer use.

Perhaps the most far-reaching improvement in the man-computer system will be achieved by advances in I/O techniques. Data-processing rate is considerably less than 10^2 bits per second for man and 10^5 or 10^6 for a modest digital computer. It was this contrast in speed that was originally the occasion for great excitement in the intellectual community. However, man is a very superior extractor of information by pattern-recognition and a rate of a few bits per second of "meaningful" information for a man (such as detection of a blip on a radar screen or understanding a spoken command) might have to be represented by tens of thousands of bits per second for the computer. The seriousness of the mismatch in speed between man and computer resulted from the fact that computers would accept inputs and create outputs only in their own terms, terms which

required the (mostly serial) delivery of all the information. Developments in I/O techniques are taking advantage of the speed mismatch and having the computer accept inputs and produce outputs in more human terms, that is, at a high order of abstraction. Several laboratories have developed photographic inputs. They use the same basic method of digitally scanning the photograph and scaling the signal according to intensity. FIDAC [121] is the best-known system. The time required to classify photographs or quantify some aspect of them has been reduced by many orders of magnitude, and fundamentally new biomedical applications have become feasible. For example, FIDAC is being used in X-ray, crystallography, electron microscopy, and analysis of radiographs, and Ledley [122] has described the use of FIDAC in measurement of chromosomes. A related development using digitized photographic input of a regular structure allows the picture to be improved by averaging transformations, simulating an old photographic technique [123].

A significantly improved microscope based on holography has been developed. Use of holography in biology represents several distinct advances: direct observation of dynamic biological phenomena is possible because optical holography has no practical limit of depth of field for most (microscopic) applications [124]; protein structures can be inferred by holographic image synthesis methods [125]. These methods are computer-based and their refinement will probably have the incidental effect of bringing closer the distant advent of general-purpose holographic I/O facilities in general biomedical computer technology.

Software for graphical output from the computer has been in use

in many systems for some years. Software packages for larger systems of the leading computer manufacturers include graphical display on an oscilloscope or digital plotter; the relatively small LINC computer had this facility. Graphical input, however, which will greatly facilitate man-computer interaction, is still being developed [126]. Full development of this technique will radically change the production of engineering drawings and consequently the whole approach to engineering planning.

A truly "conversational" man-computer interaction awaits further advances in I/O techniques utilizing acoustic signals. Early, crude devices for automatic speech recognition were produced by Smith [127]. Work is going on in a handful of laboratories, but no method has reached the stage of allowing practical verbal control of a computer. Likewise, although synthetic production of complex sound spectra under precise computer control is quite feasible [128] and speech sounds are synthesized by computers at Bell Telephone Laboratories, this technique has not developed to the point of practical communication in man-computer systems. Analysis of these systems and concern for their improvement leads naturally to the strategy of "humanizing" the computer by endowing it with pattern-recognizing capacities. This in turn leads to fundamental questions about the mechanisms of human pattern recognition and intelligence, as discussed earlier in this section.

The development of time-sharing, large, cheap, rapid-access memories, and more conversational man-computer interaction leads naturally to the growth of an "Information System," a multi-purpose men-machine system, rather than man-machine system. Such a system is used to store, manipulate,

organize, and display large amounts of data to allow its human users to communicate with each other, to perform routine organizing and clerical functions as an aid to problem-solving, to monitor critical variables, and perhaps perform other more demanding tasks. For example, computer-based hospital information systems are being developed for handling patient records, performing laboratory tests and recording the results, optimizing use of hospital facilities such as the operating rooms, aiding physicians in diagnosis, and monitoring critical physiological variables such as oxygen saturation during surgery. Such large information systems were described in Section IV-E.

G. Summary

The future of computers in medical and biological engineering will certainly bear out a trend already evident in research and clinical applications today--larger, faster, and more flexible machines must evolve to stem the data deluge from the systems under study. The computers that appear to be needed for the future fall into three categories.

(1) Large-scale hardware-oriented machines used for data processing; specifically, information processing and retrieval, statistical analysis, and numerical calculations.

(2) Hybrid computers with large-scale digitally controlled analog complements, fast interface equipment, and medium-size digital complements. Since these computers would carry the system simulation load the digital complement should be hardware-oriented and also have a sophisticated interrupt capability.

(3) Experiment-oriented machines typified by a compact process

control computer used as an experiment-computer interface for a computer such as outlined in (1) above. This PC machine could function also as the digital half of a hybrid system, although its main purpose would be to pre-process data for a larger computer.

V. ENGINEERING PHYSICS

Since all the skills of engineering science are being exercised in the solution of biomedical problems, a discussion of this interconnection can follow a traditional curricular outline: mechanics of rigid and deformable bodies, mechanics of fluids, heat light, sound, electricity, magnetism, materials, nuclear physics--all areas of engineering physics which interface with biological studies. In addition, systems theory sheds light on many biological subjects, and these will be handled separately in Section VI.

A. Mechanics

Biomechanics studies the forces acting on human and animal bodies or body parts and their resulting motions. In its application it is concerned with man-machine mechanical coupling, manipulators, bone and joint prosthesis, orthopedics, vehicular safety, and many other analysis and design problems.

The structural and mechanical properties of skin, bone, and cartilage have been studied by Kenedi [129], Zarek [130], Gaynor Evans [131], and others. Analysis of complex procedures, such as forces exerted during walking, are being studied by Contini, who also provides a current list of references [132], [133].

Analyses, both linear and nonlinear, of anatomical viscoelastic structures have been made, often using analog or digital computers. For example, the nonlinear elasticity and complex structure of the lens capsule [134] gives the accommodative control system many of its most significant properties. When applied to blood vessel walls [135] - [138], biomechanical analysis yields pressure and flow relationship; the inverse of this mathematical model provides the physician with diagnostic information about vascular disease from pressure and flow measurements. (This model will appear again in Section V-B. Determining the contractility of cardiac and skeletal muscle and the length-tension relationship is part of a more basic problem involving the dynamics of motion of a distributed mechanical system.

B. Fluid Mechanics

The flow of air in respiratory passages will be discussed from the system's viewpoint in Section VI. The other studies of fluid flow in biological structures relate to the circulatory system. Two theories of dynamics of arterial circulation have been proposed: (1) Windkessel's theory [139] - [142] and, (2) Womersley's theory [141] - [147]. The Windkessel theory is based on the intermittent and transient nature of the pressure and flow pulses. On the other hand, Womersley's theory advocates emphasis on the repetitive and cyclic nature of arterial flow and pressure, and thus has many fruitful analogies in the electrical circuit theory, e.g., impedance analogy and traveling-wave theory. Most of the present research in this area is oriented towards Womersley's theory [147], [151].

Studies done by Haynes and Burton [145], [147], [148], [151] on the nature of the non-Newtonian behavior of blood indicate that the dynamic behavior of blood in each element of the circulatory system at normal driving pressures is essentially linear. Prothero and Burton [145], [149], [151] have investigated the nature of capillary flow using micropipetts and millipore filters. Their results were as follows:

(1) The plasma between the two red cells in bolus flow has a peculiar"circus motion."

(2) The bolus flow greatly accelerated the equilibrium with hemoglobin.

(3) The important function of mixing in the capillaries isachieved by bolus flow without any appreciable hemodynamic cost.

Fich and Welkowitz [135] have proposed a tapered reflectionless model of the aorta. The resultant equations are nonlinear partial differential equations which can be solved by making appropriate approximation. Apter's model [136] of the aorta is a set of nonlinear ordinary differential equations which are solved on an analog computer. Further research should be conducted on

(a) study of branching pulsatile flow in flexible tubes,

(b) non-Newtonian nature of blood flow,

(c) theoretical study of capillary flow,

(d) instrumentation for pressure and flow measurements.

C. Heat, Light, and Sound

Besides the systems and cybernetics involved in whole body temperature

regulation, other aspects of thermics are being applied to human physiology. Heat transfer studies of the skin and of stationary and flowing blood are vital to the design of heat exchange apparatus for hypothermic procedures [152] and for implanted power sources [153]. Relationships between the functional state of visceral organs and the intensity of infrared radiation from certain parts of the body have been studied in the Soviet Union since 1962 [154], [155] as well as in the United States [156]. An interesting aspect of microwave diathermy is the electrical excitation produced at molecular levels. It has long been known that the macromolecule is influenced by its groups in the microwave field even when the frequency is removed from the relaxation frequency of that macromolecule [157]. Quantum microwave explanations may be in order, even though the energies are much lower than those considered in the usual ionizing radiation studies [158].

Some interesting work in microwave biology is currently being done by Schwan. From his earlier work in studying the electrical properties of human tissue, it has been possible to determine physical parameters, such as reflection and absorption coefficients and cross sections.

The direct application of optics and acoustics to research in vision and audition predates the emergence of bioengineering by some centuries, and has remained generally in the physiological literature. This is not true of the cybernetic view of visual and auditory systems, and so these areas of bioengineering study are included in Section VI.

Other connections between heat, light, and sound, and bioengineering are chiefly concerned with measurement and visualization of internal organs and were described in Section IV.

D. Electricity

Static electric field theory is one of the engineering sciences that is most frequently applied to biological problems, especially to those of electrocardiology and electroencephalography. In the heart, depolarization of excitable cells produces local currents which spread through the passive, conductive tissues of the torso and are manifested at the surface by time-varying potential differences. Many interesting aspects of field theory arise. There is the "forward" problem, in which a postulated set of current sources produces a potential distribution on a surrounding insulating surface. This problem has been vigorously attacked by groups from Duke University [159] and others [160]. The irregularity of the boundary, lack of homogeniety in the medium, and an isotropic conduction in muscular tissue make the problem an interesting one.

Another fruitful approach to the relationship between cardiac generators and electrocardiographic body voltages has stemmed from volume conductor measurements in torso models. Here one inserts a current source of known orientation, strength, and location, and physically measures the voltages produced. The vectorcardiographic lead systems in use at the present time were designed on the basis of such measurements. Invoking the Helmholtz principle of reciprocity, Brody. and Arzbaecher [164] used an alternative measurement technique wherein electrodes on the surface of the model are energized and cardiac-region voltages are measured. In the early days of electrocardiology, the spread of electrical activation in the heart was modelled by a fixed

position, variable direction current dipole; electrocardiographic registration of this dipole was accomplished by lead systems with simple vectorial properties. Geselowitz [162] proposed a model containing multipolar components as more representative and is presently designing a lead system for extracting the quadrupole; the electrocardiographic registration of quadrupolar and octapolar components is accomplished by lead systems with second- and third-rank tensor properties, as has been shown by Brody and his co-workers [163], [164].

The inverse problem, computing source distribution from external potentials, has also been the subject of much work [161], [165]. Here the problem is made more interesting because instead of a unique solution, there are an infinite number of solutions. One must constrain the solution so that it is mathematically neat or physiologically satisfying or both. In Horan's work [165], one sees a graphic example of an approach to this inverse problem. An excellent review of this entire subject was given by Plonsey as a tutorial lecture at the 19th Annual Conference on Engineering in Medicine and Biology, November 1966.

Aside from field theory, other electrical concepts have been useful in bioengineering. The electrical properties of living tissue, the phenomenon of electrode polarization, and the notion of biological impedance are all involved in design of the prosthetics mentioned in Section II. Schwan has examined the effect of frequency on linearity. The use of an impedance measurement for volume studies is a common practice, and plethysmographic instruments employing this principle were mentioned in Section I. Indeed, biomedical instrumentation is the chief area of interaction between biomedicine and the electrical aspects of engineering physics.

The magnetic properties of living tissues, the magnetic fields produced by body currents and the biological effect of external magnetic fields have never been regarded as very important areas of bioengineering research. Inductive effects are small because the electrochemical currents produced by cell membrane depolarization as well as their time derivatives are small. Nevertheless, McFee and Baule, Cohn, and others have obtained magnetocardiograms of high quality with a signal-to-noise ratio only slightly inferior to an EKG. A Rumanian group has recently used high frequency magnetic fields to reduce the infectivity and hemagglutinating potential of influenza virus [166]. Electromagnetic flowmeters clamped around the aorta of experimental animals are in general use.

E. Materials

The greatest impetus to the engineering study of materials from a biological viewpoint has come from the development of prosthetic devices for surgical implantation and temporary extra-corporeal systems for circulatory, respiratory, or renal assistance, described in Section II.

Materials introduced into the body may be chemically and mechanically unstable or toxic. They may induce cancer, clotting, or foreign body reactions. Various applications of synthetic polymers have been reviewed by Halpern [168], Autian [169], and Sears [170]. Levine [167] predicts that combining certain polymers with heparin will probably be a basis for further development of anti-thrombic surfaces and discusses the often-observed effect on clotting of surface electrical charge.

A vascular prosthesis of Teflon and Dacron is in general use and

knitted Dacron is presently an indicated prosthesis for arterial replacement [171]. The inert plastic used for plastic surgery is basically silicone rubber. Teflon has been used for prosthesis of the middle ear due to its many suitable characteristics for sound conduction. In the area of general surgery, tantalum and stainless steel have been used for suturing materials. Materials such as stainless steel and vitallium have been used extensively in the area of general orthopedic surgery.

F. Atomic and Nuclear Physics

The areas of radiation physics that have been of most interest to bioengineers are those of hospital radiology and tracer-isotope studies. The therapeutic aspect of radiology in cancer treatment takes advantage of sophisticated dosimetric calculations. Digital computer techniques both for implanted sources and external beams now assure maximum local concentration with a close control on scattered and unwanted skin dosage.

It is expected that the diagnostic aspects of radiology will also become computer-oriented, to allow some automatic processing of the vast amount of roentgenographic data being produced.

The use of radioisotopes in tracer studies has been of interest to bioengineers because of the instrumentation involved and the necessity for mathematical analysis of the results. Body or organ compartmental calculations are complicated by mixing, dilution, radioactive decay, body uptake, transit time, and other effects.

An isolated example of the new application of nuclear studies to bioengineering is the work of Pilkington using spin echo nuclear magnetic resonance to measure blood flow [172].

VI. CYBERNETICS OR SYSTEMS SCIENCE

A. Control

Cybernetics was defined by Wiener as the "science of control and communication in animals and machines" [173]. It is in this area of bioengineering that some of the most exciting scientific contributions have developed. Of all biological control systems, the neurological control systems most often conform to such important systems analysis requirements as unidirectional transmission between casually related lumped parameter elements. By this we mean that information passes unidirectionally, undisturbed by backward interaction, from one block to the next; and that each block in a block diagram represents an operation or mathematical transformation that can be considered as being located at a node or in one point, that is lumped, rather than spread over real physical dimension.

A classical example of a neurological control system is the pupillary servomechanism [174]. Here the feedback path can be experimentally opened using either optical or electronic techniques. Both linear transfer function analysis, including stability, oscillations, and noise and, as well, the sophisticated and nonlinear engineering theory such as Weiner-G functional analysis [175], have been successfully applied. All the knowledge in engineering control theory could be brought to bear on this one relatively primitive neurological reflex. As will be explained in Section VII, the requirement for advanced engineering science in the applications in biology is one of the important educational roles of bioengineering. Exciting and intellectually substantial thesis problems for engineering students can be generated.

Many other neurological reflex systems have also been studied; in particular, those controlling the movement of the eyeball in either versional tracking movements or vergence movements have resulted in interesting applications of engineering theory. The manual control field has been similarly developed in a number of directions, in addition to that of practical applications in the design of airplanes and space vehicles. Neurological models of the control elements and the neuromuscular and sensory elements of the hand movement system have been used to attempt a rational parameter nonlinear model of the system [177]. Both the eye and hand movement system exhibit characteristics such as discontinuous or sample data operation, predictive ability for repetitive input signals which are quite different from the noisy unpredictive, nonlinear pupillary system.

B. Information Theory

The nervous system is also amenable to analysis in terms of information theory. An interesting example is the use of Shannon's information theory [178] to analyze the nerve impulse code in the simple crayfish tail light-receptor system [179].

The general approach to the central nervous system, considering it as an assemblage of neurons performing logical operations, has been stimulated by the pioneering work of McCulloch [180] and his three students, W. Pitts, J. Lettvin, and P. Wall. Their work on various portions of the nervous system acting as transformation operators or property filters is exemplified by work on the frog's retina [181]. This is an important, experimental illustration of cybernetics for bioengineering,

for engineering science, and for classical neurophysiology. The McCulloch-Pitts neuron will be discussed later as an example of "bionics." More classical neurophysiologists, such as J. Eccles, R. Granit, and others, have become interested in the brain as a computer. Recent work on anatomical transfer functions for the cerebellum [182] shows an extension of engineering science into the field of anatomical relationships.

C. Physiology, Biophysics, and Biochemistry

The systems approach has an important interface with analytical physiology both in the understanding of physiological control and in the development of formal mathematical engineering models. Of biological control systems, the cardiovascular system is one of the most important. It has many subtle features, such as distributed transmission line elements and complex mechanical constraints. Attinger, McDonald, and Noordergraaf [183] study a more realistic cardiovascular system modeled on the bases of real pulsatile flow, the branched arterial tree, the veins, and the heart as components in the entire cardiovascular system. Rideout [184] uses the two-fluid scheme for simulation of gas transport in blood and the perturbation method for study of dye flow dynamics, using a complex hybrid computer system in conjunction with his studies. Harris [185] is interested in a systems identification method for determining parameters of central circulation from clinical indicator dilution curves in patients with intracardiac shunts. Warner [186] is also involved with a similar type of parameter estimation from indicator dilution curves for circulation pattern under various stages

of anesthesia and with various drug effects. His aim is to reflect the response of the vascular system to demonstrate the role which different vascular beds have in the cardiovascular mixing process. Stacy, Coulter, and Peter [187] have been studying power dissipation in vascular networks. These are based on measurements of arteriovenous pressure differences and flows in pulmonary and systemic vascular beds. Data are recorded on magnetic tape and processed using a LINC computer complex. Impedance and phase angle determinations show that mean power dissipation sometimes overestimates actual power dissipated. Energy cost of transport appears to be a very sensitive indicator of cardiovascular performance. Other studies produce sinusoidal oscillatory flows of blood in rigid cylindrical tubes and pressure gradients are obtained. Hydraulic impedance versus frequency curves for blood differ significantly from those of aqueous glycerol, and from predictions of Womersley's [188] theory. These studies on the cardiovascular control indicate the complexity of this system, prospects for application of systems science to cardiovascular physiology, and the importance of various engineering instrumentation and computation techniques in these studies.

The respiratory system begins to be involved as soon as one considers the cardiovascular system. A review of the respiratory system modeling by Horgan [189] starts with Grodin's [190] classical work and reviews six recent papers studying the respiratory system, including his own work. Stacy and Peters [191] also have studied lung compliance. Other interesting biocontrol systems are the endocrinological control

system, the temperature control system, and fluid balance. It is clear that even an overview such as this status report attempts cannot even mention a single research activity in each of these interesting fields.

On the one hand, physiology without biophysics and biochemistry remains largely engineering systems science applied to biology; on the other hand, important interfaces exist between cybernetics and both biophysics and biochemistry. Even though biophysics and biochemistry represent analysis of elements of physiological systems, much of the research in these fields requires systems analysis to place it in proper perspective. Muscle and nerves are themselves complex systems, and non-linear circuit models of muscle [192] attempt to carry models beyond those proposed by such physiologists as Huxley [193] and Wilkie [194] by utilizing engineering analysis. In addition to modeling neurons from the point of view of their role as information operators, as illustrated by the McCulloch-Pitts neuron model discussed in Section VI-E, there is also interest in modeling single neurons in terms of their membrane properties, as in the model of Geisler [195]. From this random-process model is indicated the necessity for a very fast recovery function for neurons in the mammalian auditory system.

Biochemical systems relate closely to endocrinological control as indicated by work by Finkelstein [196] and by Campbell and Abbrecht [197] in terms of pancreatic response and control of blood glucose level. A recent interesting article by Chance et al. [198] relates to the chemical feedback mechanisms in glucose metabolism. Here we have an interaction between engineering theory and the metabolic machinery of the cell.

Biochemical control systems lead to interface between cybernetics and molecular biology. Here the term the genetic "code" is obviously an attempt to make analogies with coding and information theory results of engineering communication science. Even more important advances will hopefully soon be made in developmental control and embryological mechanisms, so that this important theoretical scientific interface should be watched with great attention.

D. Medicine

The scientific aspects of medicine are just beginning to benefit from the systems approach. Many, if not most, diseases have pathophysiological mechanisms which might be classified not as a breakdown in single elements, but rather in the loss of control in proper operating interaction of a system of elements. This concept offers a long-range promise in the basic understanding of disease mechanisms. The more applied interaction of bioengineering and medicine in terms of computerized diagnosis and automated information processing was discussed in Section IV.

The interface of systems science with biomathematics has developed into quite a vigorous one. Several training programs of bioengineering cooperate with biomathematics programs. The importance of classical applied mathematics and of statistics cannot be minimized, and the work of such people as Rashevsky, Landlahl, and Bartholomay [199] in further developing biomathematics programs related to bioengineering has been an important influence; however, many feel that engineering mathematics is the exciting applied mathematics of the present day.

At this point, two important goals for bioengineering should be identified. One is the conceptual insight into communication and control

processes in biology utilizing the systems approach. The other is the conceptual insight into the basic nature of disease processes from the point of view of cybernetics. These two goals are suitable for focusing of attention for planning efforts or for closely watching the future development of bioengineering.

E. Bionics: Computer Design and Pattern Recognition

Bionics, or, as Professor McCulloch prefers, biomimetics, has been defined by Steele of the Air Force as the utilization of principles of design of biological systems for the construction of man-made devices. One of the most exciting developments in this field occurred in the mid 40's when Von Neumann, Goldstine, Bigelow, and Burks utilized McCulloch-Pitts neurons to design the Institute for Advanced Study digital computer. McCulloch and Pitts had developed the formal neuron as a "poverty-stricken" example abstracted from the richness of normal brain neurons, in order to analyze in terms of Boolan algebra the properties of networks of such neurons [200]. Von Neumann, in carrying out the logical design of this digital computer in which logical design was separated in principle from hardware design, used McCulloch-Pitts neurons to draw his logical diagrams [201]. The names given to various portions of the computer, such as the memory organ and the logical organ, are other more intuitive examples of the application of principles of design of biological systems to the construction of an important artificial device. Other areas of importance in biomimetics are recent developments of artificial robots, such as those designed to operate in lunar environments, utilizing principles of postural and manual control, as elucidated in human engineering studies.

Another exciting bionics area is the development of artificial intelligence pattern-recognition devices for visual pattern-recognition in the directions both of hardware devices and also of digital computers,

as exemplified by the artificial intelligence programs for pattern-recognition analysis of electrocardiograms [202]. First is the problem of the selection and measurement of properties of an event or object to be recognized. The sum total of these properties and their scale of measurements constitutes the reality of an event. Each event thus is transformed into a point in N-dimensional property space. If certain events occur repetitively and cluster in a particular region of this property space, they will be recognized as dissimilar. Another of the problems in building a self-adaptive or self-organizing pattern-recognition device or program is to make appropriate decision rules for partitioning the space appropriately to create a taxonomy. The third problem area is the use of this categorized space or taxonomic classification for some purpose such as signal identification. This bionic pattern-recognizer is a good example of the development of engineering design principles from analytical and experimental studies of principles of function of biological organisms [203].

VII. EDUCATION

Bioengineering educational programs, besides their primary direction, are having an influence in medical and life science education and in engineering schools.

A. Health Sciences

At the present time, the medical world is in a crisis. Developments in mathematics, physics, and engineering sciences have outstripped the

understanding of general practitioners, medical students, and even members of academic medical faculties. For this reason, such important institutions as the National Institutes of Health in Washington are turning increasing attention to the "continuing scientific development" of the medical scientist in terms of re-education of senior medical people and faculty personnel who have already demonstrated creative ability in their own fields. For this re-education, bioengineering, biomathematics, and physics loom large. The bioengineering programs in some universities are already intimately related to these developments in medical education, and represent a national resource for such re-education.

It has now become apparent also that it is necessary to restructure the general process of medical education. Just as the Flexnor Report developed an undergraduate program preceding medical school and revolutionized and set the stage for the present situation, so too the studies by Brown, Dow, and Dickson may change the present status of the graduate education phase of medicine. If in 1900 it was important to introduce chemical science into medicine, so too in the 1970's it will be equally important to incorporate engineering system science into the medical curriculum. Bioengineering, playing intellectually an essential role in physiological research and teaching, will already be present in the medical school curriculum and will be an excellent base upon which to build in two directions. The first direction is towards more graduate-level mathematics, engineering, and physics for medical students. The second direction is towards practical interaction with the technological world of instrumentation, computers, and systems science that will be the

dominant influence in the delivery of medical and health services to patients in hospitals and in the community.

B. Bioengineering Education

At the present time, bioengineering has an exceedingly difficult educational task. Almost all programs are required to have three tracks in their educational curriculum. These are: (1) re-education of the biologist stressing background mathematics, physics, and engineering science; (2) education of the engineer in the basic principles of biology and the experimental approach to the richness and variety of biological systems; and (3) the bioengineering subjects themselves covering advances in the field over the past 15 years, now becoming semistructured with the experience of many programs. These bioengineering subjects, of course, require preliminary background in both biology and engineering.

There are also two levels of graduate education in the field of bioengineering. At the first level, the aim is to produce a bioengineer capable of participating in an interdisciplinary team effort in some bioengineering project. He might be a biologist or physician immersed in some problem area who wishes to obtain enough engineering background to be able to communicate with professional engineers. He might be an engineer who wishes to master only enough physiology background to be able to communicate effectively with the life scientist and is willing to depend upon him for definition of the problem area in either applied or basic research. A few programs have now developed at the master's degree level to produce individuals with this training; there is

obviously a great need for such a person in increasing the technological level of the medical and health sciences.

Most of the programs already supported by the NIGMS have as their goal a Ph.D. student who will be able to serve as an independent scientist, either as a faculty member or as a leader of a bioengineering group in industry or in government. He must have enough biology background to be able to specify, define, and have good scientific intuition about a biological or medical problem area and at the same time have enough engineering background so that he is able to appreciate the ever-new developments in engineering theory and be fully up to par as a doctoral-level engineer in applying engineering science to these problems. In short, he must be an independent scientist with excellent background in two quite different fields.

The difficulties of such programs are great. Edmonson [204] describes one such program at the University of Michigan. An interesting suggestion is that of O. Schmitt, who proposed modular education wherein video-tape lectures would be obtained from experts in specific areas. In this way, a group of people scattered throughout the country, that no one university could possibly collect, would be able to provide material for a solid program in bioengineering.

Another solution to the problem of bioengineering education, and one about which one may be particularly enthusiastic, is the undergraduate program in bioengineering. It seems quite possible to have a student major in engineering, and in particular, for example, in electrical or information engineering, fully satisfying all engineering core

requirements, his major requirements, and his engineering minor requirements. In addition, he can use his elective time to obtain all the biological and chemical background that would be required of a biology major or of a premedical student. Even in a rather rule-conscious state university, a capable student should be able to complete the bioengineering program in the usual four years. Perhaps one should stress the need for that flexibility which would enable him to approach two different subjects such as biology and engineering. For such a student, the bioengineering graduate program will be relatively straightforward. He may use his time not to get biological background but to take more advanced biology graduate courses; similarly, if his engineering background obtained as an undergraduate makes unnecessary the engineering remedial courses, he can take graduate engineering courses which will keep him fully abreast of the developments in engineering science. He will also immediately have the prerequisite for taking the bioengineering courses and will be able to obtain a rather complete background in a number of contemporary aspects of bioengineering. This will also give him an advantage in choosing a thesis topic early, and developing it into a major scientific contribution.

C. Engineering Science

Bioengineering is a two-way street and in education has made considerable contribution to the development of engineering science. It does this by being a source of thesis problems. Many engineers who are not particularly interested in bioengineering find it profitable to do their doctoral thesis work, or undergraduate and graduate projects,

in the life science field because of the severe test that the life sciences place on the application of engineering theory. Much of the problem of engineering education, with the increasing attention given to complex mathematical analysis, is to find interesting real systems of enough complexity to test modern theory. Thus, there exists clear utility for bioengineering as a schooling ground for these engineering science principles.

In any case, engineering is encompassing more and more aspects of the descriptive sciences--it now plays an essential role in physics and biology and is beginning to play an important role in sociology and linguistics. A hopeful side of bioengineering training is that with the further development of engineering and system science, especially in such fields as control, communication, and information, it looks as if all the sciences will become more unified and more interrelated. All sciences use input-output descriptions, study materials, and energy-conversion principles and share common tools such as instrumentation and computers for model-building. In this way, the unity of the descriptive sciences--physics, chemistry, biology, psychology--is becoming clearer as they share more and more the common structure of systems engineering science.

VIII. GOALS

Although this section is entitled "goals," several aspects of bioengineering are included: problems of an interdisciplinary field, possible solutions,

a general discussion, as well as nine goals, identified and suggested as foci for planning efforts.

A. Problems

It might be well to consider some of the problems of the bioengineering field at this point. We have already mentioned that bioengineering has two main aspects: one, building instrumentation and other engineering devices for biology and medicine; the other, the analysis of complex biological systems by means of the application of engineering science. In addition, bioengineering is split in several other ways. The academic area, with its emphasis on the application of engineering science to biology and medicine and the development of far advanced instrumentation, is to be contrasted with the rapidly developing bioengineering industry, with its proper concentration on state-of-the-art instrumentation and systems for the delivery of health services. In addition, there is the rather complicated contrast between the physical sciences and the biological sciences. Most engineers feel at home with such physical sciences as physics and chemistry; when they enter the biological or life sciences realm, there is an added factor of complexity and variability of data, which hinders their ease of entry into bioengineering. Conversely, there is difficulty for the biological scientist to acquire those habits of rigorous theoretical approach and precise experimental measurement that characterize the physical sciences and indeed the new area of bioengineering. Some of these problems are implied in the word "interdisciplinary."

Bioengineering as an interdisciplinary field has advantages in

that it attracts imaginative scientists from a number of fields. Recently, students of science as a process have emphasized the flow of scientific ideas in the actual movement of individual people in and out of different scientific fields and from one geographical location to another. Bioengineering certainly profits from such mobility of its adherents and practitioners which, when added to their imagination and ability, has made the field the exciting area that it is.

However, there are problems of any interdisciplinary area which bioengineering shares. For the academician, this means that there is a less clear route for him to follow, less chance of an established department protecting and developing his research and academic development. There are many political difficulties which take various forms in different universities and teaching hospitals which occupy and distort a good deal of the activities in bioengineering. In the more active universities, these problems are at times circumvented by imaginative university and teaching hospital leadership. For example, the late S. Talbot, an early bioengineer, with a Ph.D. in physics, was appointed an Associate Professor of Medicine at the Johns Hopkins Medical School. Similarly, M.D.'s have been appointed Professors of Engineering at some engineering schools. That this is not more widespread indicates some of the difficulties bioengineering faces. Professional societies in some scientific fields are very well organized and contribute to self-critical abilities of a discipline. The multiplicity and disorganization of professional societies in the bioengineering field require that many less able people are in important policy roles, and it is difficult

for the field to provide rapid critical scientific feedback to its members' contributions. This is emphasized in the diffuse literature in which bioengineering material is now being published and the resultant decrease in the feedback of a critical referee's review that provides for the positive development of the field. This feedback for excellence is much less certain in the bioengineering field than in some more established disciplines.

Finally, we find that the need for education in depth must continually be emphasized as opposed to a superficial training in either engineering or biology for the individuals who are bioengineers.

The interaction between academic bioengineering and the rapidly burgeoning biomedical engineering industry has also suffered because of lack of the well-established pathways that would exist if bioengineering were a recognized departmental discipline with a well-trained, homogenous, intercommunicating professional cohort. Dr. G. Bugliarello has suggested that a study be made to:

> "determine effectiveness criteria for biomedical engineering research, so as to translate such research into economic value. In shaping effectiveness criteria, considerations such as the number of persons affected by disease and the gross national product increases, realizable through restoration of health to this group, may be of considerable importance. It has been estimated that developments resulting from biomedical engineering research will result in formation of a billion-dollar

industry in the next decade. Balanced against these economic advantages must be the cost of training and supporting superior research personnel, as well as the cost of supporting research.

"On the basis of the effectiveness criteria, the study should try to determine priorities for the research dollar investment. It should attempt to estimate the total level of support required for an effective biomedical engineering research program. An estimate of the present and future potential of the interaction of technology and the life sciences should be included. In calculating this potential, considerations of the present levels of bioengineering commitment and of bioengineering training are important. Also important is an investigation of how more effective coupling of engineering and medical activities can be achieved. Certainly this study must not neglect to consider the overall dimensions of the health problem in determining how to maximize bioengineering effectiveness."

B. Goals

It seems worthwhile at this point to list nine exciting areas; each seems to be at a focus of effort and support and therefore should be watched closely for development in the near future.

(1) The clinical application of new transducers is a most

important aspect in the elucidation of pathological processes, in diagnostic measurement, and in the delivery of health services. What is needed is the education of a larger group of physicians who understand the three aspects of the advance that bioengineering can provide, including instruments to make objective measurements, computers to perform the mathematical analysis necessary for understanding these complex medical measurements, and finally the concepts that clarify the physiological and pathophysiological systems. The next step, which is one that the medical community must undertake, is to work to apply this instrumentation, computation, and conceptual advance to the clinical area. This involves integrating the new information with the old by means of careful clinical studies. The medical doctor must understand the vocabulary of bioengineering, but he may very well expect to be aided by rapidly developing "standards for instrumentation" which will guarantee him performance, reliability, and safety of these new devices, for which he cannot, of course, assume responsibility. Also, a great deal of research is now going on to discover useable energy sources within the body, to develop long-term implantable energy storage elements, or to transmit energy from some convenient external energy source. Telemetering to and from passive sensory transducers is a live possibility.

New transducers such as the ultrasound image converters may provide large amounts of medical information previously unavailable. In any event, clinical application of new sensory and control transducers will certainly be one of the advancing areas of bioengineering.

(2) Complex instrumentation systems such as intensive care monitoring systems for post-operative, seriously ill, and acute trauma patients involve much more than just a collection of sensory and control transducer instruments.

It involves a combined systems arrangement with proper display of ongoing measurements in a form useful for humans to interpret. Often digital or hybrid computer systems are involved. Other examples are control of operating room anesthesia and other variables as well as physiological monitoring of the patient during operations and control of such instrumentation as heart/lung pumps. Another example of a complex instrumentation system involving the computer would be an automatic analytical chemical laboratory. Not only is a great deal of work going on in industry to provide "state-of-the-art" systems for the delivery of health care, but a good deal of bioengineering research in the broadening and sophistication of these systems is also proceeding. For example,

the development of automatic physical diagnosis of neurological control systems by measurement of reflexes, muscle tone, eye movement, and visual function using computer-controlled instrumentation would be a valuable addition to screening laboratories that now rely mainly on biochemical and clinical laboratory tests. This is exciting because it involves the interaction of industry, hospitals, medical personnel, bioengineering technology--all integrated into an applied science development of national importance for the delivery of health services.

(3) Prosthetics have come a long way since the wooden leg of Peter Stuyvesant. This important area involves the use of proper biomaterials with performance criteria matching or surpassing those of biological materials and with little or no toxic effects. In addition to limb prosthetics, artificial hearts and artificial kidneys are occupying the interest of many bioengineering groups throughout the country. It is clear that we can expect a great deal of these areas, although much important basic scientific and applied bioengineering research remains to be done before reliability and adequate performance are obtained.

(4) Non-numerical uses of digital computers will rapidly increase under the pressure of high costs of human intelligence for doing a variety of complex tasks. Just as most banks now keep checking accounts by computer, so

pattern-recognition in the diagnosis of electrocardiograms, electroencephalograms, and, especially important, two-dimensional picture pattern-recognition, will be done by computers in the future. The use of computers for making diagnoses, given patient historical information, physical signs, and laboratory data, seems to be an area where computers, with their ability to handle very low probability information in an effective way, will soon be very much more valuable than the present research efforts now indicate. Both pattern-recognition and diagnosis research are now justified mainly in terms of their clarification of processes involved, their educational value in postdoctoral medical education, and only in an ancillary fashion, for their ability to handle practical information-processing loads. However, once they demonstrate potential performance, growth should be rapid because of the high cost and scarcity of trained medical and scientific personnel as contrasted with the enormous demand for high-quality medical services.

(5) Hospital information systems based on large-scale digital computers have been preceded by smaller computers, mostly in the financial area of inventory control, payroll, and patient billing during the past five years. The next goal is numerical patient data, such as biochemical laboratory results. Interesting developments in the use of

operations research techniques for obtaining fuller bed occupancy, more active use of scarce and expensive facilities such as surgical rooms, and reducing queuing with resultant loss of patient time and comfort for procedures such as X-rays, also look promising at the present. Advanced research on non-numerical hospital information system data, such as verbal medical records, involves information-retrieval problems and may have to await both another generation of digital computers with larger-sized associated memories and more facile man-machine communication, as well as new scientific and engineering ideas, concepts, and approaches. The interaction with the human must proceed with more and more emphasis made on making it easy for the human to communicate with the computer to obtain meaningful data in organized and logical displays. Bioengineering research in all of these areas is actively going on in universities, teaching hospitals, and industry.

(6) Cybernetics, the conceptual insight into control and communication processes in biology, has been and promises to continue to be one of the leading intellectual areas in the field of bioengineering. In addition to the exciting scientific discoveries, the research in this field also acts as a stimulus for the development of engineering theory and generates thesis problems approachable by the application of systems science.

(7) Disease may be termed the pathophysiology of control: slower in development, but certainly in the long run important in medicine, is the use of systems theory to obtain conceptual insights into disease itself. Pathophysiological mechanisms appear to be largely loss of control of various developmental, biochemical, and physiological mechanisms in the body under the influence of disease. Thus, systems science may be a unifying principle and approach leading to the understanding of medicine itself as a scientific field. It may rationalize the study of medicine and place in proper perspective the overwhelming detail of abnormal mechanisms present in various individual diseases.

(8) Education is an activity which in a certain sense controls the future development of any field. Bioengineering is playing an important role in terms of re-education of medical academicians who have already demonstrated important scientific productivity and leadership but have been somewhat left behind in terms of the new technology. Simultaneous changes are urgently needed in the medical curriculum to prevent rapid obsolescence of the present generation of students. Bioengineering might well be the focus for the injection, however painful, of additional mathematics, engineering, and systems science into the medical curriculum. Young physicians will

emerge into a world of medicine which is in large part dominated by complex engineering instrumentation systems and some familiarity with bioengineering will enable them to assert adequate human judgment in dealing with the results of information generated in this machine environment. They will then be able to take their place with independent biomedical scientists, able to deal with the technical world of science in applying it to medical problems.

Another phase of bioengineering education that should develop during the next period is the development of much more appropriate bioengineering courses. The field has been hampered, as mentioned earlier, by the lack of adequate training of bioengineers who come from either one or the other of the biological or engineering fields. Now that a new group of students with adequate bioengineering backgrounds is being developed in many graduate and undergraduate programs throughout the country, courses appropriate for people sophisticated in both biological and engineering sciences can be developed. These will clearly be more advanced, more sophisticated, and yet in a way simpler and logically organized because of the lack of necessity for remedial, pedagogical efforts. An example of such a course is a course in biological servomechanisms, which is discussed in the body of this report.

A hopeful side of these educational problems is that systems science is in some fundamental way unifying the scientific fields instead of adding another subspecialty. The techniques and approaches of systems science form an introduction to all the mathematical and applied-mathematical techniques developed in the various branches of science and mathematics and provide a unified approach to the descriptive sciences such as biology, chemistry, and physics which are each describing natural phenomena at different levels of organization.

(9) The scientific literature of bioengineering will require a good deal of cohesive growth. This may be provided by more abstracting services, which will cover the wide range of journals in which bioengineering literature is appearing. More important is the development of critical reviews of different areas in bioengineering. This will accelerate the normal feedback for excellence that the scientific literature provides for in any scientific field. This is perhaps an important goal that can be strengthened by a group effort. It is most necessary to provide proper advice to contracting agencies of the United States government for supporting bioengineering in a wide variety of project-oriented and pure science directions, as well as for helping medical and hospital personnel without background in making equipment purchases.

C. Possible Solutions

The NIH, in particular the NIGMS, has a number of mechanisms for aiding in the development of a field such as bioengineering.

(1) The individual scientist. By means of fellowship support at all levels of the educational process, the NIH has supported bioengineering. A particularly important aspect is the special fellowship for persons with more mature backgrounds wishing to re-enter the academic scene for that further training often most necessary in interdisciplinary fields.

The young research scientist as a junior faculty member needs support for his research work in amounts of $10,000 to $30,000 a year, which should be rather freely available without much background experience and past work justification. If a scientist is willing to devote all of his research time, approximately 50 percent after his teaching and perhaps clinical duties are provided for, he might reasonably be allowed an annual amount approximately equal to one to two times his salary for several years. After that period, further research grants should be based upon his past productivity and upon his ability to generate exciting research plans for the future. Most of these funds would be used for graduate students, technicians, and the shared costs of running joint facilities, such as computer time. This mechanism allows for

growth of a field based upon the imagination of the able young people within it, unfettered by "overall plans" of senior scientists. It would be a great mistake for the NIH to abandon this approach in favor of concentrating large amounts of funds in the hands of university or hospital organizations or senior scientists.

(2) Cooperative programs and facilities at levels of $100,000 to $300,000 a year are, however, very important in developing more coherent research than that possible in terms of support of one research scientist and his students. An example would be the program-project support of a group working in hemodynamics, where several faculty members might band together to do both basic research on hemodynamics and, as well, applied work on improvement of heart-lung machines. Such support would also provide local political strength to ease the problem of identification of this interdisciplinary field in the university and teaching hospital.

Training programs are appropriately discussed in this area, both because of their general size and the need here for cooperation amongst a number of faculty members with perhaps a responsible leader sparking the program. These programs have been an important factor in the recent rapid growth of bioengineering and its gradual increase in scientific and engineering merit through the years.

(3) "Centers of excellence" with budgets of approximately $1,000,000 a year are important in terms of arranging for leadership in achieving important national goals such as those nine identified in the previous section. For example, a center for bioengineering research in cybernetics might be located at a major engineering school possessing an advanced, integrated engineering research group. Here would be located facilities in terms of on-line digital computers and a large enough group of active bioengineers to be able to attract international notice and visitors from all over the nation and the world. It could serve as a focus by holding national meetings; other individuals, while doing independent, noteworthy work in their own university, could draw upon the resources of the center of excellence for help and stimulation.

Another example would be a "regional health computer center" with large-scale computer facilities in a bioengineering context, which could develop new methods and test feasibility of proposed methods of handling large amounts of data for a whole region's health problem.

Educational experiments could be conducted in a center for excellence: for example, evaluation of the modular education concept proposed by Prof. O. Schmitt, wherein a number of individuals contribute

short courses in their own field of expertise. A center would be able to have the audio-visual resources to accumulate and integrate such educational material and, even more importantly, test out its effectiveness using the modern methods of educational research. Such a center might also have responsibility for literature surveying, abstracting, and critical reviewing.

Another center of excellence might have primary responsibility for testing biomedical engineering instrumentation both in the engineering laboratory and in the hospital setting. This might be a much less expensive and more effective mechanism than setting up a special government department, as the Food and Drug Administration, which controls pharmaceutical agents. Another center or several centers might be involved in the delivery of health services dealing with complex instrumentation systems, hospital information systems, on-line monitoring automatic laboratories, and other developments mentioned in the previous section on goals.

D. Discussion

The general philosophy of our attempts to solve the problems of bioengineering should not be either a preponderance of planning or an argument for anarchy, but rather, as Dr. J. Wiesner has indicated, a

"planning for anarchy." By this he meant the planning for the provision of resources such that independent scientists and individual universities could strengthen their efforts, generate further resources, and interact in the rather free and probabilistic way that characterizes the scientific community. An example might be not to try to force a single biomedical engineering society on all of the workers in this field, but rather to arrange for intersociety contacts and to use the dissemination of information and re-education to bring varying groups together by attracting them, rather than by attempting to force the issue.

The way in which government, universities, and industry have indeed interacted and cooperated during the past ten years as the field of bioengineering has developed is remarkable. It appears that the NIH has had, and still has, a catalytic role to play, stimulating with individual research grants, with training programs, and with larger centers, so that the field of bioengineering may develop even more rapidly in the future, contributing its scientific creativity and technological developments to the patient care and scientific responsibilities of medicine.

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